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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/718,316	11/20/2003	Ian Francis Hassan	4-30843D	9782

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/718,316	HASSAN ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 16-20* is/are rejected.

7)☒ Claim(s) *14,15 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of US 10/262,408, filed 10/01/2002, which is a continuation of US 09/942,805, filed 08/30/2001, which is a continuation of PCT/EP00/01722, filed 03/01/2000.

Applicant's amendments filed September 23, 2004 have been entered. The addition of claim 21 in amendments filed September 23, 2004 is acknowledged.

Claims 1-21 are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13, and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Briggner et al. (US Patent 5,874,063) in view of Gennaro et al. (Remington's Pharmaceutical Sciences, 1990, 18th edition, page 1699-1701, and 1706-1707), O'Connor (Pulmonary Pharmacology & Therapeutics, 1998;11:397-399), Sequeira et al. (US Patent 5,837,699), and Sequeira'393 (WO95/20393). Briggner et al., Gennaro et al., and Sequeira et al. are references of record in the parent application.

Briggner et al. teaches that inhalation drugs including β2-agonist such as formoterol fumarate dihydrate, and steroids such as mometasone may be formulated

into a mixture of the both agents in a finely divided dry particulates with a median diameter from 0.1 to 10 μm (See particularly claims 1, 7; also col. 2, line 1-6; col.5, example 6). Briggner et al. also teaches one pharmaceutical carrier useful for formulating the composition is lactose (See claim 9).

Briggner et al. does not expressly teach to use particularly mometasone to be employed in the inhalation formulation composition. Briggner et al. does not expressly teach that the composition would be in an aerosol forms and dispersed in halogen-substituted hydrocarbon propellant. Briggner et al. does not expressly teach the dosage and the weight ratio of formoterol fumarate dihydrate and mometasone to be 3 to 36 μg of formoterol and 25 to 800 μg of mometasone herein. Briggner et al. does not expressly teach the composition of formoterol fumarate dihydrate and mometasone could be separated into unit dosage forms in a pharmaceutical kit. Briggner et al. does not expressly teach the method of treating airway inflammatory disorder.

Gennaro et al. teaches that steroids could be formulated into aerosol, in which the steroids are dispersed in the propellant with a median diameter of 3 to 6 μm. (See particularly 1706, col. 2, third paragraph). Gennaro et al. also teaches the fluorinated hydrocarbon propellant 114 and propellant 114a are commonly used in aerosol dosage form (See page 1699, col. 2 second paragraph to page 1700, col. 2).

O'Connor teaches that employment of the combination of β-agonist and steroids in the management of asthma is more effective than that of either agent alone (See page 397, col. 2, last paragraph to page 398, col. 2, fourth paragraph). O'Connor also teaches that the addition of β-agonist, salmeterol, to fluticasone regimen resulting in a

greater improvement in asthma control than increasing the dose of fluticasone alone (See page 398, col. 1, last paragraph). O'Connor also teaches that formoterol, combining with a steroid compound, budesonide, in low dose would produce an equal effect as the high dose budesonide (See page 398, col. 2, second paragraph).

Sequeira'393 discloses a method of treating respiratory inflammatory disorders such as asthma by administering a composition comprising the known steroidal anti-inflammatory agent, mometasone furoate in a pressurized oral inhaler to the patient (See, e.g., page 3, lines 16-19, page 10 lines 2-5). Moreover, it discloses that mometasone can be used as adjuvant therapy with bronchodilators in a therapeutic composition (See page 10, lines 5 and 9). Sequeira'393 also discloses the use of chloroflorocarbon propellants broadly as well as the use of non-chloroflorocarbon propellants with or without surfactants in the said inhaler (See page 10, lines 19-21).

Sequeira et al. teaches that the effective dosage range for mometasone would be 25μg to about 800μg for treating asthma (See particularly col. 4, line 21-47, claims 4 and 8).

It would have been obvious to one skill in the art when the invention was made to employ 25 to 800μg of mometasone and 3 to 36μg of formoterol into an aerosol dosage form, dispersed in fluorinated hydrocarbon propellant in a medicament composition and separate the composition into unit dosage forms in a pharmaceutical kit. It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the formoterol-mometasone composition in a method of treating asthma.

One of ordinary skill in the art would have motivated to employ 25 to 800μg of mometasone and 3 to 36μg of formoterol into an aerosol dosage form, dispersed in fluorinated hydrocarbon propellant in a medicament composition and separate the composition into unit dosage forms in a pharmaceutical kit because both 25 to 800μg of mometasone and 12μg of formoterol are known to be useful in treating asthma. Therefore, combining two agents which are known to be useful to treating asthma individually into a single composition useful for the very same purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069. Moreover, formoterol is known in use with a steroid in a method of treating asthma. It is also known that combining a long-acting, inhaled β2-agonist with an inhaled glucocorticoid led to a greater improvement in the control of symptoms and in lung function than doubling the dose of the inhaled glucocorticoid. Therefore, combining any known steroids, including mometasone, with fomoterol would have been reasonably useful in a composition of treating asthma.

Furthermore, one of ordinary skill in the art would be reasonably expect to formulate formoterol-mometasone combination composition into a different inhaled dosage forms such as aerosol composition by dispersing the actives herein into a commonly used propellant, including fluorinated hydrocarbons. Reformulation of the known actives composition into a separate unit dosage form and place them into a pharmaceutical kit is within the purview of skilled artisan.

In addition, one of ordinary skill in the art would have been motivated to employ the formoterol-mometasone composition in a method of treating asthma. As taught in O'Connor and Sequeira'393, formoterol, when combine with a steroid, is useful in

treating asthma and mometasone is also known to be useful in treating asthma. Therefore, concomitantly administering both formoterol and mometasone, which is known as effective in treating asthma individually and in combination, together for treating asthma is *prima facie* obvious (*In re Kerkhoven* 205 USPQ 1069).

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, the data presented in declaration of by Dr. Fromond filed April 5, 2002 in the parent application 09/942,805 have been considered and are found persuasive in regard to the presence of unexpected result of the combination of 1.5μg/kg of formoterol and 30μg/kg of mometasone. However, the evidence of unexpected results must be of a scope reasonably commensurate with the scope of the subject matter claimed. The claims herein are not limited to the synergistic amount of formoterol and mometasone. Furthermore, the data presented in the declaration filed September 23, 2004 demonstrating the unexpected synergy in the combination of formoterol and mometasone have been considered, and are found persuasive. However, claims 1-13

and 16-20 are not commensurate with the scope of the data presented. Therefore, only claims 14, 15, and 21 are found allowable.

Response to Arguments

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). When taking the cited prior arts as a whole, one of ordinary skill in the art would have been motivated to combine the teachings of the cited prior arts to arrive at the instant claimed invention.

Applicant's arguments filed September 23, 2004 averring the cited prior art's failure to provide motivation to combine the cited prior arts' teachings because of the structural, chemical, and pharmacological differences between the herein cited compounds. Applicant is merely arguing, without factual basis, the structural, chemical, and pharmacological differences between the herein cited compounds and that of the cited prior art would lead to difficulties in formulating the herein claimed composition. It is not clear how these differences would become problems in terms of formulating the composition. Without such evidence, applicant's arguments are not persuasive and are treated as non-factual based arguments.

Applicant's arguments filed September 23, 2004 with regard to Sequeira's teachings have been considered, but are not found persuasive. The arguments are

directed to the delayed "clinical use" of formoterol, which is not what the claims directed to. Argumetns directed to unclaimed limitations are considered moot.

Applicant's arguments averring the instability of formoterol leading to unobviousness of putting formoterol and mometasone together have been considered, but are not found persuasive. Again, there is no data as to the stability of formoterol present in the instant case. Furthermore, the composition containing formoterol is known and patented. The reasons why the FDA not approved formoterol for treating asthma might not be relevant to the patentability of the herein claimed composition. It is no way to know because there is no evidence provided in the instant case pointing out such relevancy between the disapproval by FDA and the patentability of the instant composition. Moreover, FDA did not approve the "method" of using formoterol to treat asthma. However, the instant claims are drawn to a "composition" containing old and well-known agents.

Allowable Subject Matter

Claims 14, 15, and 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617